

WHAT IS CLAIMED IS:

- 1 1. A DNA molecule, which encodes a body weight modulator, or a fragment  
2 thereof, selected from the group consisting of:
  - 3 A. the DNA sequence of FIGURE 1 (SEQ ID NO:1);
  - 4 B. the DNA sequence of FIGURE 2 (SEQ ID NO:2);
  - 5 C. DNA sequences that hybridize to any of the foregoing DNA  
6 sequences under standard hybridization conditions;
  - 7 D. DNA sequences that code on expression for an amino acid sequence  
8 encoded by any of the foregoing DNA sequences;
  - 9 E. degenerate variants thereof;
  - 10 F. alleles thereof; and
  - 11 G. hybridizable fragments thereof.
- 1 2. An isolated nucleic acid molecule, which nucleic acid molecule encodes an  
2 ob polypeptide, which polypeptide is characterized by having about 145 to about  
3 167 amino acid residues, being expressed predominantly by adipocytes, and being  
4 capable of inducing a reduction of body weight in an animal.
- 1 3. The isolated nucleic acid of Claim 2, wherein the ob polypeptide has an  
2 amino acid sequence selected from the group consisting of the sequence depicted  
3 in Figure 3 (SEQ ID NO:2), Figure 3 from amino acid number 22 to amino acid  
4 number 167, Figure 4 (SEQ ID NO:4), Figure 4 from amino acid number 22 to  
5 amino acid number 167, Figure 5 (SEQ ID NO:5), Figure 5 from amino acid  
6 number 22 to amino acid number 166, Figure 6 (SEQ ID NO:6), and Figure 6  
7 from amino acid number 22 to amino acid number 166.
- 1 4. The nucleic acid molecule of Claim 2 selected from the group consisting of  
2 DNA and RNA.

- 1 5. The nucleic acid molecule of Claim 2, which has a sequence as shown in  
2 Figure 1 (SEQ ID NO:1) from nucleotide number 46 to nucleotide number 550.
- 1 6. The nucleic acid molecule of Claim 2, which has a sequence as shown in  
2 Figure 2 (SEQ ID NO:2) from nucleotide number 46 to nucleotide number 550.
- 1 7. The nucleic acid molecule of Claim 1 which is detectably labeled.
- 1 8. A cloning vector, which comprises the DNA molecule of Claim 1.
- 1 9. An expression vector, which comprises the nucleic acid molecule of Claim  
2 2, operatively associated with an expression control sequence.
- 1 10. The expression vector of Claim 9, wherein said expression control  
2 sequence is selected from the group consisting of the cytomegalovirus hCMV  
3 immediate early gene, the early or late promoters of SV40 or adenovirus, the lac  
4 system, the trp system, the TAC system, the TRC system, the major operator and  
5 promoter regions of phage  $\lambda$ , the control regions of fd coat protein, the promoter  
6 for 3-phosphoglycerate kinase, the promoters of acid phosphatase, and the  
7 promoters of the yeast  $\alpha$ -mating factors.
- 1 11. A probe capable of screening for a nucleic acid encoding an ob polypeptide  
2 in alternate species, which probe is a labeled DNA molecule of Claim 1.
- 1 12. A unicellular host transfected with a cloning vector of Claim 8.
- 1 13. A unicellular host transfected with an expression vector of Claim 9.
- 1 14. The unicellular host of Claim 13 wherein the unicellular host is selected  
2 from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeasts,

3 CHO, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, and BMT10 cells, plant  
4 cells, insect cells, and human cells in tissue culture.

1 15. An ob polypeptide, which polypeptide is encoded by the DNA molecule of  
2 Claim 1.

1 16. An ob polypeptide, which polypeptide is characterized by having about 145  
2 to about 167 amino acid residues, being expressed predominantly by adipocytes,  
3 and being capable of inducing a reduction of body weight in an animal.

1 17. The ob polypeptide of Claim 16 which has the amino acid sequence shown  
2 in Figure 3 (SEQ ID NO:2) or Figure 5 (SEQ ID NO:5).

1 18. The ob polypeptide of Claim 16 which has the amino acid sequence shown  
2 in Figure 4 (SEQ ID NO:4) or Figure 6 (SEQ ID NO:6).

1 19. An immunogenic fragment of an ob polypeptide, which polypeptide is  
2 characterized by having about 160 amino acid residues, being expressed  
3 predominantly by adipocytes, and being capable of inducing a reduction of body  
4 weight in an animal.

1 20. The immunogenic fragment of an ob polypeptide of Claim 19, which is  
2 selected from the group consisting of

3 Val-Pro-Ile-Gln-Lys-Val-Gln-Asp-Asp-Thr-Lys-Thr-Leu-Ile-Lys-Thr (SEQ  
4 ID NO:18);

5 Leu-His-Pro-Ile-Leu-Ser-Leu-Ser-Lys-Met-Asp-Gln-Thr-Leu-Ala (SEQ ID  
6 NO:19);

7 Ser-Lys-Ser-Cys-Ser-Leu-Pro-Gln-Thr-Ser-Gly-Leu-Gln-Lys-Pro-Glu-Ser-  
8 Leu-Asp (SEQ ID NO:20); and

9 Ser-Arg-Leu-Gln-Gly-Ser-Leu-Gln-Asp-Ile-Leu-Gln-Gln-Leu-Asp-Val-Ser-  
10 Pro-Glu-Cys (SEQ ID NO:21).

- 1 21. An antibody to the ob polypeptide of Claim 15.
- 1 22. An antibody to the ob polypeptide of Claim 16.
- 1 23. A method for preparing an antibody to an ob polypeptide, comprising:
  - 2 A. conjugating the immunogenic fragment of an ob polypeptide of
  - 3 Claim 19 to a carrier protein;
  - 4 B. immunizing a host animal with the ob polypeptide fragment-carrier
  - 5 protein conjugate of step A admixed with an adjuvant; and
  - 6 C. obtaining antibody from the immunized host animal.
- 1 24. An antibody to an ob polypeptide prepared according a method comprising:
  - 2 A. conjugating an immunogenic fragment of an ob polypeptide of
  - 3 Claim 19 to a carrier protein;
  - 4 B. immunizing a host animal with the ob polypeptide fragment-carrier
  - 5 protein conjugate of step A admixed with an adjuvant; and
  - 6 C. obtaining antibody from the immunized host animal.
- 1 25. The antibody of Claim 21, 22, or 24 comprising a polyclonal antibody.
- 1 26. The antibody of Claim 21, 22, or 24 comprising a monoclonal antibody.
- 1 27. An immortal cell line that produces a monoclonal antibody according to  
2 Claim 26.
- 1 28. The antibody of Claim 21, 22, or 24 labeled with a detectable label.
- 1 29. The antibody of Claim 28 wherein the label is selected from the group  
2 consisting of enzymes, chemicals which fluoresce, and radioactive elements.

- 1 30. A method for measuring the presence of an ob polypeptide in a sample,  
2 comprising:
- 3 A. contacting a sample suspected of containing an ob polypeptide with  
4 an antibody that binds to the ob polypeptide under conditions which allow for the  
5 formation of reaction complexes comprising the antibody and the ob polypeptide,  
6 B. detecting the formation of reaction complexes comprising the  
7 antibody and ob polypeptide in the sample;  
8 in which detection of the formation of reaction complexes indicates the presence of  
9 ob polypeptide in the sample.
- 1 31. The method of Claim 30 in which the antibody is bound to a solid phase  
2 support.
- 1 32. The method of Claim 31 which further comprises contacting the sample  
2 with a labelled ob polypeptide step (A), and removing unbound substances prior to  
3 step (B), and in which the formation of reaction complexes in the sample is  
4 detected by observing a decrease in the amount of labelled ob polypeptide in the  
5 sample.
- 1 33. The method of Claim 31 which further comprises contacting the sample  
2 with a labelled antibody in step (A), which labelled antibody is an anti-ob  
3 polypeptide antibody, and removing unbound substances prior to step (B), and in  
4 which the formation of reaction complexes in the sample is detected by observing  
5 an increase in the amount of labelled antibody in the sample.
- 1 34. The method of Claim 30 in which an ob polypeptide is bound to a solid  
2 phase support.
- 1 35. The method of Claim 34 which further comprises contacting the sample  
2 with an ob polypeptide in step (A), and removing unbound substances prior to step  
3 (B), and in which the antibody is labelled and the formation of reaction complexes

4 in the sample is detected by observing a decrease in the amount of labelled  
5 antibody.

1 36. A method for evaluating the level of ob polypeptide in a biological sample  
2 comprising

3 A. detecting the formation of reaction complexes in a biological sample  
4 according to the method of Claim 30; and

5 B. evaluating the amount of reaction complexes formed, which amount  
6 of reaction complexes corresponds to the level of ob polypeptide in the biological  
7 sample.

1 37. A method for detecting or diagnosing the presence of a disease associated  
2 with elevated or decreased levels of ob polypeptide in a mammalian subject  
3 comprising:

4 A. evaluating the level of ob polypeptide in a biological sample from a  
5 mammalian subject according to Claim 36; and

6 B. comparing the level detected in step (A) to a level of ob polypeptide  
7 present in normals or in the subject at an earlier time;  
8 in which an increase in the level of ob polypeptide as compared to normal levels  
9 indicates a disease associated with elevated levels of ob polypeptide, and decreased  
10 level of ob polypeptide as compared to normal levels indicates a disease associated  
11 with decreased levels of ob polypeptide.

1 38. A method for monitoring a therapeutic treatment of a disease associated  
2 with elevated or decreased levels of ob polypeptide in a mammalian subject  
3 comprising evaluating the levels of ob polypeptide in a series of biological samples  
4 obtained at different time points from a mammalian subject undergoing a  
5 therapeutic treatment for a disease associated with elevated or decreased levels of  
6 ob polypeptide according to the method of Claim 36.

- 1 39. The method according to Claim 37 or 38, wherein the disease associated  
2 with elevated levels of ob polypeptide is selected from the group consisting of  
3 AIDS, cachexia, cancer, and anorexia nervosa.
- 1 40. The method according to Claim 37 or 38, wherein the disease associated  
2 with decreased levels of ob polypeptide is selected from the group consisting of  
3 obesity, Type II diabetes, hypertension, and elevated blood lipids.
- 1 41. A test kit for measuring the presence or amount of ob polypeptide in a  
2 sample, comprising:  
3 A. an anti-ob polypeptide antibody of Claim 21, 22, or 24;  
4 B. means for detecting binding of the anti-ob polypeptide antibody to  
5 ob polypeptide in a sample;  
6 C. other reagents; and  
7 D. directions for use of the kit.
- 1 42. A method for changing the body weight of a mammal comprising inhibiting  
2 the expression of an ob polypeptide encoded by a nucleic acid of Claim 2.
- 1 43. The method according to Claim 42 comprising expressing an antisense  
2 nucleic acid molecule hybridizable to a nucleic acid that expresses the ob  
3 polypeptide, expressing a ribozyme that cleaves a nucleic acid that expresses the  
4 ob polypeptide, administering an antisense nucleic acid molecule hybridizable to a  
5 nucleic acid that expresses the ob polypeptide, and administering a ribozyme that  
6 cleaves a nucleic acid that expresses the ob polypeptide.
- 1 44. A pharmaceutical composition for reducing body weight of an animal  
2 comprising the ob polypeptide of Claim 15 and a pharmaceutically acceptable  
3 carrier.

1 45. A pharmaceutical composition for reducing body weight of an animal  
2 comprising the ob polypeptide of Claim 16 and a pharmaceutically acceptable  
3 carrier.

1 46. A method for reducing the body weight of an animal comprising  
2 administering an amount of a pharmaceutical composition of Claim 45 effective to  
3 reduce the body weight of an animal to an animal believed to be in need of  
4 decreased body weight.

1 47. The method according to Claim 46 wherein the animal is a human, and the  
2 ob polypeptide is human ob polypeptide.

1 48. A method for reducing the body weight of a mammal comprising increasing  
2 the expression of a protein encoded by the nucleic acid of Claim 2.

1 49. A pharmaceutical composition for increasing the body weight of an animal  
2 comprising an antagonist of an ob polypeptide.

1 50. The pharmaceutical composition of Claim 49, wherein the antagonist is  
2 selected from the group consisting of an antibody that binds to and neutralizes the  
3 activity of ob polypeptide, a fragment of the ob polypeptide that binds to but does  
4 not activate the ob receptor, and a small molecule antagonist of the ob  
5 polypeptide.

1 51. A method for increasing the body weight of an animal comprising  
2 administering an amount of the pharmaceutical composition of Claim 49 effective  
3 to cause an increase in body weight to an animal believed to be in need of  
4 increased body weight.